amended in order to expedite prosecution. The claim now includes a recovery step and is believed to overcome the rejection. Reconsideration is requested.

The Examiner also indicated that claims 17 and 18 were in improper Markush format, and required that full terminology be used for "LHRH" in the claims. Claim 17 has been amended and is believed to be in acceptable form, and "LHRH" has been changed to "luteinizing hormone releasing hormone" where it appears in the claims. It is believed that all of the 35 USC § 112, second paragraph rejections have been overcome.

The Examiner has maintained the rejection of claims 12-19 under 35 USC § 103 as being obvious over Callahan et al. in view of Finkenaur and further in view of Reissman et al, Moore, Yoshikawa et al., Brown et al. Stewart et al. or Kornreich et al. This rejection is traversed for the following reasons.

The present inventors have solved the problem of how to produce a pharmaceutical formulation containing gel forming peptides for parenteral administration. In USP 23, page 1650, which is attached for the Examiner's convenience, it is indicated that injections should meet the requirements for sterility. Therefore, a sterilization step must be carried out. Since peptides are unstable, a steam sterilization by autoclaving in the final container is not feasible. Therefore, a sterile filtration must be performed. The process of such a sterilization is also described in USP 23,

at pages 1978-1979, including the requirement of using a membrane filter rated 0.2 mm or 0.22 mm. The problem with this procedure lies in the fact that aqueous solutions of gel forming peptides cannot pass through these filters due to gel formation. Therefore, the required sterilization of such substances is not possible by filtration.

The present inventors have solved this problem by dissolving the gel forming peptide salt in aqueous acetic acid (claim 12). Under these conditions, a sterilization by filtration of such a solution can be carried out. It is noted that the invention uses peptide salts, as for example the acetate salt, to be dissolved in aqueous acetic acid. The invention is not a method of producing the acetic acid salts of said peptides, but rather a method for the preparation of sterile lyophilizates.

None of the cited references discloses or suggests a method for the preparation of a sterile lyophilizate of a gel forming peptide salt. In the cited references, only methods for the preparation of acetate salts or methods for purification of peptide salts are disclosed. The compounds disclosed in the references represent the starting materials for the present process.

Callahan et al. (US 4,908,475) relates to new vasopressin compounds but not LHRH analogs such as cetrorelix. A method of preparation of the new compounds is also described. In order to purify the peptide, the compound was extracted with

120 ml of 10% HOAc and 120 ml of 1% HOAc. In this case only the peptide acetate was formed in an aqueous solution. The use of an aqueous acetic acid solution in order to dissolve the peptide salt to avoid gel formation is not described.

Reissmann et al. (Cancer Research and Clinical Oncology Vol. pp 44-49 No. 1 1992) only describe pharmacological results with cetrorelix trifluoroacetate and cetrorelix acetate utilized as bulk substance and not as a sterile lyophilisate. A process for preparing a sterile cetrorelix lyphilisate is not described in this article.

Moore (US 4,711,877) relates to new cyclic peptides with a structure similar to vasopressin and not to LHRH analogs. After the peptide is eluted from a column with pyridine acetate buffer the residue is removed in vacuum and the residue is lyophilized from 10% acetic acid. There is no description of how to prepare a sterile lyophilisate using a peptide which usually will change into the undesired and unfilterable gel form.

Kornreich (4,701,499) teaches how an N-substituted peptide can conveniently be dissolved in diluted acetic acid and then lyophilized. Korneich does not describe how to make a sterile filtrate and lyophilisate from a gel forming peptide salt.

Yosikawa (US 5,268,360) describes opioid peptides received from hydrolysis of wheat proteins. The peptides were liberated from the resin, the solvent (hydrogen fluoride) was

distilled off and the residue was extracted with 30% acetic acid and lyophilized. In this patent there is no part which shows difficulties caused by filtration process in order to produce a sterile final product.

Brown (US 4,372,884) describes peptide which inhibit the secretion of pituitary gland growth hormone. The peptide material was eluted from a Bio Rex-70 resin column with pyridine acetic acid water or 50% acetic acid. The fractions were diluted with water and lyophilized. There is no teaching how to prepare a filterable peptide solution using acetic acid.

For all of the above reasons, it is submitted that the presently claimed invention is not obvious from the cited references, either alone, or in combination. Withdrawal of the 35 USC § 103 rejection is respectfully requested.

All rejections having been addressed, it is respectfully submitted that this application is in condition for allowance, and Notice to that effect is respectfully requested.

Respectfully submitted,

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